I. AMENDMENT

Amendments to the Specification:

Please replace the paragraph beginning at line 18 of page 2 with the following amended paragraph:

Purely on empirical grounds, Edward Jenner first demonstrated protective vaccination against infectious disease in the 1790s. After observing that milkmaids did not contract smallpox, he intentionally infected a boy with cowpox then subsequently found him immune to smallpox. Since then, vaccines against measles, polio, anthrax, rabies, typhoid fever, cholera and the plague, have been developed. The methods of developing new vaccines vary and differ for each virus, bacteria, or other pathogen target; however, they have traditionally consisted of whole pathogens in an attenuated or killed form, as did Jenner's vaccine. Both social and economic considerations make vaccination the optimal method for protecting animals and humans against disease or death. However, vaccines have not been developed for many of the most serious human diseases, including Malaria, tuberculosis, HIV, respiratory syncytial virus (RSV), *Streptococcus pneumoniae*, rotavirus, Shigella and other pathogens. There is a need to develop effective vaccines, yet for many pathogens vaccines are not readily produced. For example, the antigenic drift of influenza virus requires that new vaccines be constantly developed. Research efforts continue to try to identify effective vaccines for rabies (Xiang *et al.*, 1994), herpes ~~(Rouse, 1995)~~; tuberculosis (Lowrie *et al.*, 1994); HIV (Coney *et al.*, 1994) as well as many other diseases or pathogens.

Please replace the paragraph beginning at line 4 of page 3 with the following amended paragraph:

Most currently available vaccines are composed of live/attenuated pathogens ~~(Ada, 1991)~~. These live inocula infect cells and elicit a broad immune response in the host. The strength of this approach is that no antigen identification is required, because all the components of the pathogen are presented to the immune system. However, this straightforward approach carries an inherent problem. Pathogenicity of the attenuated strain or reversion to virulence is possible. At best, components of the pathogen that are not needed for the protective immune response are carried as baggage; alternatively some components may compromise protective immunity. Pointedly, pathogens become pathogenic by evolving or acquiring factors to defend themselves against or avoid a host immune system. In whole organism vaccines, the repertoire of antigens and their expression levels are controlled by the pathogen. Consequently, the host immune system is often not directed to the most protective antigen determinants. Another consideration is that presentation of all antigens of a pathogen provides opportunities for the unprotective ones to cause deleterious side effects such as autoimmunity or toxicity.

Please replace the paragraph beginning at line 23 of page 5 with the following amended paragraph:

The etiologic agent of Lyme disease is a spirochete bacterium of the *Borrelia* genus. *Borrelia burgdorferi* predominates in the U.S. but *Borrelia garinii* and *Borrelia afzelii*, as well as others, are common in Europe (Rahn, 2001). Human infection occurs through a zoonotic route. The white-footed mouse and the white-tailed deer serve as bacterial reservoirs in the U.S., since they are favored sources of blood meal for the deer-tick (*Ixodes scapularis*). Transmission of the Borrelia spirochete to humans occurs following a bite from an infected tick (Gayle and Ringdahl, 2001). In 1990, less than 8,000 U. S. cases of Lyme disease were reported to the CDC. However by 1999 the number had jumped to 16,273 cases (Gayle and Ringdahl, 2001). Endemic areas, mostly in the northeastern, mid-atlantic, and north-central states, suffer incidence levels of 1% to 3% of the population, according to the CDC. The namesake of the disease comes from the town of Lyme, Connecticut; in which a cluster of infections surfaced as juvenile rheumatoid arthritis cases in 1975 (Thanassi and Schoen, 2000). While the disease is

geographically focused, surveys show that incidence is spreading. Demographically, children under 15 years of age and adults over 30 show the greatest number of infections. It has been estimated that from seven-fold to twelve-fold more infections than reported occur but are undiagnosed (Van Solingen and Evans, 2001). If the infecting tick bite is not noticed then the subsequent illness can be difficult to identify as Lyme disease because of the variability of initial symptoms and lack of serological testing standards. It has three stages that begin days to weeks following a tick bite and is characterized by an expanding skin lesion, and is sometimes accompanied by flu-like symptoms. Approximately 60% of infected individuals develop intermittent episodes of arthritis several weeks after the bite (Thanassi and Schoen, 2000). The rash and the initial arthritis resolves in a few days or weeks, however if untreated the spirochetes spread to other sites such as the host central nervous system, heart, or joints. Treatment of early stage infection with antibiotics such as amoxicillin or doxycycline usually results in the return of an individual to normal health; however later treatment is less effective in eliminating disease. Antimicrobial therapy of disseminated Lyme Borreliosis for as much as three months may not be sufficient to eliminate spirochetes or prevent relapses (Hercogova, 2001~~ and Steere *et al.*, 2001~~). During the middle stage, the inflammatory manifestations of the disease develop into meningitis, cardiac blockage, or arthritis. In late stage disease months or years following initial infection, spirochetes are usually not detectable but malaise continues. This may consistent of chronic arthritis, neurologic abnormalities, acrodermatitis chronica atrophicans, or other complications (Kornacki and Oliver, 1998). Infection with *B. burgdorferi* also causes moderate to severe arthritis in dogs, hamsters, mice, monkeys, and rats (Poland and Jacobson, 2001 and Croke *et al.*, 2000). It is hypothesized that symptoms are a consequence of a continued host immune response either to the cleared bacterium or against a tissue autoantigen. Borrelia mimicry of a self-antigen has been shown to activate this T-cell mediated immunopathology that is perpetuated (Trollmo *et al.*, 2001). A particular HLA (-DR4) subtype, which is found in a third of the population, has been correlated with individuals that develop persistent arthritis (Rahn, 2001). The proposed autoimmune mechanism has implications for the utility and safety of a Lyme vaccine. For example, any vaccine that engenders a host immune response that resembles those responses stimulated by a Borrelia infection might cause disease. An additional consideration for vaccine design is that previous infection does not appear to prevent reinfection, indicating that long-term immunity is not engendered by the whole bacterium (Rahn, 2001).

Please replace the paragraph beginning at line 15 of page 8 with the following amended paragraph:

The mechanism of immune action appears to be the production of high-titer antibodies specific for a conformational epitope of OspA from *B. burgdorferi* sensu lato. After LYMErix was released, it was shown that yearly boosters, following the three-dose immunization series, are required to maintain antibodies at adequately high levels (Thanassi and Schoen, 2000). The randomized vaccine efficacy trial was tested where only *B. burgdorferi* sensu lato is found. The ability of LYMErix to cross-protect against the heterogeneous subspecies and different Borrelia species is unknown. An experiment in mice with an OspA carrying a small number of amino acid changes showed no cross-protection. Another concern is that the highest risk group, children under 15, is not approved to receive this vaccine (Poland and Jacobson, 2001). Although vaccine recipients reported no unusual levels of arthritis during the 20-month phase III trial, several case studies subsequent to the report have raised concerns of vaccine-induced molecular mimicry (Rose *et al.*, 2001). Chronic Lyme arthritis has been associated with increased OspA reactivity in synovial fluid. Evidence has been presented that recombinant OspA priming can induce severe destructive arthritis in hamsters after spirochete infection (Croke *et al.*, 2000). The removal of ~~LYMERrix~~LYMErix from the market this year occurred because of poor sales, which may be attributed to public concern over long term efficacy and possible adverse autoimmune effects from the OspA antigen. Currently, no Lyme vaccine is commercially available.

Please replace the paragraph beginning at line 3 of page 9 with the following amended paragraph:

More recently, the tertiary structure of the OspA protein has been studied with the idea of designing a more broadly protective version of the variable antigen ~~(Luft *et al.*, 2002)~~. However whether the cited problems are real or perceived, the development of a new product that is both more effective and publicly accepted is likely to require a non-OspA composition. The rationale for having a vaccine is the documented increase in Lyme disease incidence, the geographic spread of the disease, the success of re-infections, and the association of disease with permanent rheumatoid or neurological symptoms.

Please replace the paragraph beginning at line 24 of page 16 with the following amended paragraph:

In various embodiments of the invention, an animal or subject is a mammal. In some cases a mammal may be a mouse, horse, cow, pig, dog, or human. Alternatively, a subject may be selected from ~~Deer~~deer, chickens, turtles, lizards, fish and other animals susceptible to Borrelia infection. In preferred embodiments, an animal or subject is a human.

Please replace the paragraph beginning at line 6 of page 18 with the following amended paragraph:

FIG. 1. ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* random expression library screen, round 1.

Please replace the paragraph beginning at line 15 of page 24 with the following amended paragraph:

For example Clone #1 has the following identities or similarities as determined by the BLAST program accessible through the National Center for Biotechnology Information website. GenBank Accession number are provided in the first set parenthesis for each entry and are each incorporated herein by reference. (AE001584) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp56, Identities = 819/819 (100%); (AE001578) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-6, Identities = 797/819 (97%), Gaps = 2/819 (0%); (AE001580) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-8, Identities = 794/819 (96%), Gaps = 2/819 (0%); (AE001575) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-1, Identities = 794/819 (96%), Gaps = 2/819 (0%); (AE001581) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-9, Identities = 796/822 (96%), Gaps = 5/822 (0%); (AE001577) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-4, Identities = 793/819 (96%), Gaps = 2/819 (0%); (AE001576) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-3, Identities = 789/819 (96%), Gaps = 2/819 (0%); and (AE001579) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-7, Identities = 780/819 (95%), Gaps = 2/819 (0%).

Please replace the paragraph beginning at line 28 on page 24 with the following amended paragraph:

In another example Clone #4 has the following identities or similarities as determined by the BLAST program accessible through the National Center for Biotechnology Information website. GenBank Accession number are provided in the first set parenthesis for each entry and are each incorporated herein by reference. (AE000785) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp25, Identities = 522/522 (100%); (AE000784) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp28-3, Identities = 488/522 (93%); and (AE000788) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp36, Identities = 467/510 (91%), Gaps = 2/510 (0%).

Please replace the paragraph beginning at line 5 on page 25 with the following amended paragraph:

In still other examples, Clone #5 has the following identities or similarities as determined by the BLAST program accessible through the National Center for Biotechnology Information website. GenBank Accession number are provided in the first set parenthesis for each entry and are each incorporated herein by reference. (AE001579) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-7, Identities = 197/197 (100%); (AE001578) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-6, Identities = 197/197 (100%); (AE001580) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-8, Identities = 193/197 (97%); (AE001576) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-3, Identities = 193/197 (97%); (AE001575) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-1, Identities = 193/197 (97%); (AE001577) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-4, Identities = 193/197 (97%); (AE001581) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-9, Identities = 190/197 (96%); and (AE001584) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp56, Identities = 177/197 (89%).

Please replace the paragraph beginning at line 17 on page 25 with the following amended paragraph:

In yet further examples, Clone #6 has the following identities or similarities as determined by the BLAST program accessible through the National Center for Biotechnology

Information website. GenBank Accession number are provided in the first set parenthesis for each entry and are each incorporated herein by reference. (AE000794) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp28-1, Identities = 860/860 (100%); and (AE000788) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp36, Identities = 691/693 (99%).

Please replace the paragraph beginning at line 23 on page 25 with the following amended paragraph:

In still further examples, Clone #10 has the following identities or similarities as determined by the BLAST program accessible through the National Center for Biotechnology Information website. GenBank Accession number are provided in the first set parenthesis for each entry and are each incorporated herein by reference. (AE001579) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-7, Identities = 644/644 (100%); (AE001577) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-4, Identities = 283/297 (95%), Gaps = 1/297 (0%); (AE001581) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-9, Identities = 278/294 (94%), Gaps = 2/294 (0%); (AF169008) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* circular plasmid cp18-2, Identities = 246/257 (95%); (AE001580) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-8, Identities = 248/261 (95%); (AE001575) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-1, Identities = 248/261 (95%); (AE001576) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-3, Identities = 200/225 (88%), Gaps = 6/225 (2%); and (AE001578) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-6, Identities = 198/235 (84%), Gaps = 6/235 (2%).

Please replace the paragraph beginning at line 5 on page 26 with the following amended paragraph:

In another example, Clone #11 has the following identities or similarities as determined by the BLAST program accessible through the National Center for Biotechnology Information website. GenBank Accession number are provided in the first set parenthesis for each entry and are each incorporated herein by reference. (AE000787) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp38, Identities = 127/127 (100%); and (AE000784) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp28-3, Identities = 106/127 (83%), Gaps = 4/127 (3%).

Please replace the paragraph beginning at line 12 on page 26 with the following amended paragraph:

In still another example, Clone #16 has the following identities or similarities as determined by the BLAST program accessible through the National Center for Biotechnology Information website. GenBank Accession number are provided in the first set parenthesis for each entry and are each incorporated herein by reference. (AE001578) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-6, Identities = 663/663 (100%); (AE001580) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-8, Identities = 658/663 (99%); (AE001576) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-3, Identities = 658/663 (99%); (AE001575) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-1, Identities = 658/663 (99%); (AE001577) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-4, Identities = 653/663 (98%); (AE001579) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-7, Identities = 648/663 (97%); (AE001581) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-9, Identities = 643/664 (96%), Gaps = 1/664 (0%); and (AE001584) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp56, Identities = 620/663 (93%), Gaps = 1/663 (0%).

Please replace the paragraph beginning at line 25 on page 26 with the following amended paragraph:

In yet a further example, Clone #18 has the following identities or similarities as determined by the BLAST program accessible through the National Center for Biotechnology Information website. GenBank Accession number are provided in the first set parenthesis for each entry and are each incorporated herein by reference. (AE000794) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp28-1, Identities = 983/983 (100%); (AE000788) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp36, Identities = 506/509 (99%), Gaps = 2/509 (0%); (AE000784) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp28-3, Identities = 452/470 (96%), Gaps = 1/470 (0%); (AE001584) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp56, Identities = 451/470 (95%), Gaps = 3/470 (0%); (AE000793) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp17, Identities = 451/470 (95%), Gaps = 3/470 (0%); and (U43414) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* linear plasmid lp16 DNA, Identities = 451/470 (95%), Gaps = 3/470 (0%).

Please replace the paragraph beginning at line 5 on page 27 with the following amended paragraph:

In still another example, Clone #19 has the following identities or similarities as determined by the BLAST program accessible through the National Center for Biotechnology Information website. GenBank Accession number are provided in the first set parenthesis for each entry and are each incorporated herein by reference. (AE001578) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-6, Identities = 964/964 (100%); (AE001579) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-7, Identities = 962/964 (99%); (AE001584) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp56, Identities = 888/915 (97%); (AE001576) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-3, Identities = 905/964 (93%), Gaps = 3/964 (0%); (AE001580) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-8, Identities = 904/964 (93%), Gaps = 3/964 (0%); (AE001575) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-1, Identities = 904/964 (93%), Gaps = 3/964 (0%); (AE001577) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-4, Identities = 898/964 (93%), Gaps = 3/964 (0%); and (AE001581) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-9, Identities = 896/964 (92%), Gaps = 3/964 (0%).

Please replace the paragraph beginning at line 18 on page 27 with the following amended paragraph:

In yet a further example, Clone #20 has the following identities or similarities as determined by the BLAST program accessible through the National Center for Biotechnology Information website. GenBank Accession number are provided in the first set parenthesis for each entry and are each incorporated herein by reference. (AE001576) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid cp32-3, Identities = 278/278 (100%); and (AE001584) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp56, Identities = 252/255 (98%).

Please replace the paragraph beginning at line 24 on page 27 with the following amended paragraph:

In another example, Clone #32 has the following identities or similarities as determined by the BLAST program accessible through the National Center for Biotechnology Information website. GenBank Accession number are provided in the first set parenthesis for each entry and

are each incorporated herein by reference. (AE001583) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp5, Identities = 130/130 (100%); (AE001582) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp21, Identities = 115/130 (88%), Gaps = 9/130 (6%); (AE000789) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp28-4, Identities = 115/130 (88%), Gaps = 9/130 (6%); and (AE000785) ~~Borrelia burgdorferi~~ *Borrelia burgdorferi* plasmid lp25, Identities = 104/122 (85%).

Please replace the paragraph beginning at line 21 on page 30 with the following amended paragraph:

Various methods of introducing an antigen or an antigen composition to a subject are known in the art. Vaccination methods include, but are not limited to DNA vaccination or genetic immunization (for examples see U.S. Patents 5,589,466, 5,593,972, 6,248,565, 6,339,086, 6,348,449, 6,348,450, 6,359,054, each of which is incorporated herein by reference), edible transgenic plant vaccines (for examples see U.S. Patents 5,484,719, 5,612,487, 5,914,123, 6,034,298, 6,136,320, and 6,194,560, each of which is incorporated herein by reference), transcutaneous immunization (Glenn *et al.*, 1999 and U.S. Patent 5,980,898, each of which is incorporated herein by reference), nasal or mucosal immunization (for examples see U.S. Patents 4,512,972, 5,429,599, 5,707,644, 5,942,242, each of which is incorporated herein by reference); virosomes (Huang *et al.*, 1979; Hosaka *et al.*, 1983; ~~Kaneda, 2000;~~ U.S. Patents 4,148,876; 4,406,885; 4,826,687; 5,565,203; 5,910,306; 5,985,318; each of which is incorporated herein by reference~~) ,687; 5,565,203; 5,910,306; 5,985,318, each of which is incorporated herein by reference~~), live vector and the like. Antigen delivery methods may also be combined with one vaccination regime.

Please replace the paragraph beginning at line 7 on page 33 with the following amended paragraph:

Polynucleotides and polypeptides of the invention may be used in conjunction with VLP vaccines. In many virus species, virus proteins are capable of assembling in the absence of nucleic acid to form so-called virus-like particles or VLPs. Similarly, the proteins which normally cooperate together with nucleic acid to form the virus core can assemble in the absence of nucleic acid to form so-called core-like particles (CLPs). The terms "virus-like particles" and

"core-like particles" will be used to designate assemblages of virus proteins (or modified or chimeric virus proteins) in the absence of a viral genome. The addition of antigenic peptide in the context of these particles may be especially useful in the development of vaccines for oral or other mucosal routes of administration (for examples see U.S. Patent 5,667,782, which is hereby incorporated by reference). In other embodiments of the invention virosome may also be used. Examples of virosome compositions and methodology can be found in U.S. Patents 4,148,876, 4,406,885, and 4,826,687, ~~and Kaneda, 2000,~~ each of which is incorporated herein by reference.

Please replace the paragraph beginning at line 26 on page 35 with the following amended paragraph:

I. Attenuated Pathogen Vaccines

Please replace the paragraph beginning at line 7 on page 36 with the following amended paragraph:

J. Killed Pathogen Vaccines

Please replace the paragraph beginning at line 6 on page 50 with the following amended paragraph:

Another synthetic or recombinant variation of an antigenic Borrelia polypeptide is a polyepitope moiety comprising repeats of epitope determinants found naturally in Borrelia proteins. Such synthetic polyepitope proteins can be made up of several homomeric repeats of any one Borrelia protein epitope; or may comprise of two or more heteromeric epitopes expressed on one or several Borrelia protein epitopes.

Please replace the paragraph beginning at line 11 on page 55 with the following amended paragraph:

In certain embodiments of the invention, an expression construct comprising an Borrelia polynucleotide or polynucleotide segment under the control of a heterologous promoter operable in eukaryotic cells is provided. For example, the delivery of an *B. burgdorferi* antigen-encoding expression constructs can be provided in this manner. The general approach in certain aspects of

the present invention is to provide a cell with an expression construct encoding a specific protein, polypeptide or peptide fragment, thereby permitting the expression of the antigenic protein, polypeptide or peptide fragment in the cell. Following delivery of the expression construct, the protein, polypeptide or peptide fragment encoded by the expression construct is synthesized by the transcriptional and translational machinery of the cell and/or the vaccine vector. Various compositions and methods for polynucleotide delivery are known (see Sambrook *et al.,* 2001; Liu and Huang, 2002; Ravid *et al.*, 1998; and Balicki and Beutler, 2002~~ and~~, each of which is incorporated herein by reference).

Please replace the paragraph beginning at line 30 on page 60 with the following amended paragraph:

For some uses, including *in vivo* use of antibodies in humans and *in vitro* detection assays, it may be preferable to use chimeric, humanized, or human antibodies. A dimeric antibody is a molecule in which different portions of the antibody are derived from different animal species, such as antibodies having a variable region derived from a murine monoclonal antibody and a constant region derived, from a human immunoglobulin. Methods for producing chimeric antibodies are known in the art. See *e.g.*, Morrison, 1985; ~~Ol *et al.*, 1986;~~ Gillies *et al.* 1989; U.S. Patents 5,807,715; 4,816,567; and 4,816,397, which are incorporated herein by reference in their entireties. Humanized antibodies are antibody molecules from non-human species that bind the desired antigen having one or more complementarity determining regions (CDRs) from the non-human species and framework regions from a human immunoglobulin molecule. Often, framework residues in the human framework regions will be substituted with the corresponding residue from the CDR donor antibody to alter, preferably improve, antigen binding. These framework substitutions are identified by methods well known in the art, *e.g.*, by modeling of the interactions of the CDR and framework residues to identify framework residues important for antigen binding and sequence comparison to identify unusual framework residues at particular positions. See, *e.g.*, U.S. Patent 5,585,089 and Riechmann *et al.* (1988), which are incorporated herein by reference in their entireties. Antibodies can be humanized using a variety of techniques known in the art including, for example, CDR-grafting (EP 239,400; WO 91/09967; U.S. Patents 5,225,539; 5,530,101 and 5,585,089), veneering or resurfacing (EP 592,106; EP 519,596; Padlan, 1991; Studnicka *et al.*, 1994; Roguska *et al.*, 1994), and chain

shuffling (U.S. Patent 5,565,332), all of which are hereby incorporated by reference in their entireties.

Please replace the paragraph beginning at line 29 on page 81 with the following amended paragraph:

Administration is in any manner compatible with the dosage formulation, and in such amount as will be therapeutically effective and/or immunogenic. The quantity to be administered depends on the subject to be treated, including, e.g., the capacity of the individual's immune system to synthesize antibodies, and the degree of protection desired. The dosage of the vaccine will depend on the route of administration and will vary according to the size of the host. Precise amounts of an active ingredient that required to be administered depend on the judgment of the practitioner.

Please replace the paragraph beginning at line 16 on page 94 with the following amended paragraph:

Readout analysis was focused on the joint diameter data, since joint swelling is a direct and quantitative measure of Lyme disease, whereas spirochete counting is indirect and often technically variable. Large joint diameters of the mice were measured at weeks 2, 3, 4, and 5 as described above. To assess disease, the changes in tibiotarsal joint diameter relative to that of baseline mice were calculated. Time course analyses of this mouse model of Lyme disease have shown that inflammation peaks between four and five weeks post-exposure ~~(Potter *et al.*, 2000)~~. The results at these time points are shown in FIG. 3. At 4-weeks PI, animals immunized with four clones (2, 16, 19, and 28) displayed reduced inflammation relative to the uninfected group at a 95% confidence level ($p<0.05$). A total of seven Borrelia gene fragments conferred reduced swelling at an 85% confidence interval ($p<0.15$) (clones #1, 2, 7, 16, 19, 26, and 28). At the 5-week time point, four groups, those immunized with clones #2, 7, 27, and 28, displayed reduced joint swelling data relative to the uninfected mice within a 95% confidence interval. A total of ten groups, those immunized with clones #1, 2, 7, 12, 16, 19, 27, 28, 31, 32, conferred ameliorated inflammation at an 85% interval.

Please replace the paragraph beginning at line 23 on page 96 with the following amended paragraph:

Homologues of the *B. burgdorferi* vaccine candidates identified in this screen are envisioned to be protective in some related Borrelia species such as ~~B. afzelii~~*B. afzilii*, ~~B. garinii~~*B. garinii*, or ~~B. hermsii~~*B. hermsii*. These homologous may have utility as antigens against these borrelia diseases. Unfortunately the genomes of these species are not sequenced. However the gene product encoded by the fragment on clone #1 (BBR01) displays 76% identity to a ~~B. hermsii~~*B. hermsii* gene available in GenBank. The ~~B. hermsii~~*B. hermsii* homolog of ~~B. burgdorferi~~*B. burgdorferi* BBR01 may carry protective capacity against ~~B. hermsii~~*B. hermsii*. Additionally, vaccination with genes from one borrelia species might heterologously protect against exposure to a different borrelia species.